lines 19-20, please delete "(Figure 8A)." and replace therewith --(8A and 8B),--;

line 21, please delete "(Figure 8B)." and replace therewith --(Figure 8C). --.

At page 414, line 18, please delete "Figure 10A)." and replace therewith --Figures 10A, 10B, 10C, 10D, and 10E).--;

line 23, please delete "Figure 10B." and replace therewith --Figures 10F and 10G.--.

At page 416, line 20, please delete "(Figure 11B)." and replace therewith --(Figures 11B and 11C).--.

At page 417, line 12, please delete "(Figure 11C)." and replace therewith --(Figures 11D, 11E and 11F).--.

In the Drawings:

Please replace the originally filed Figures 1A-B, 2A-B, 3, 4A-C, 5A-B, 6, 7a-b, 8a-b, 9a-b, 10a-b and 11a-c with the Formal Drawings of Figures 1A-B, 2A-D, 3, 4A-C, 5A-B, 7A-1-A-2 and 7B, 8A-C, 9A-B, 10A-G and 11A-F submitted herewith.

REMARKS

Amendments to the Specification

The majority of the amendments being made in the specification merely correct the references to the Figures such that they conform with the figure labels of the Formal Drawings. All amendments that do more than correct reference to Figures are discussed in more detail below.

Grammatical errors have been corrected by the amendment of the word "shows" on pages 24 and 26, lines 19 and 20 respectively, to "show".

We have removed reference to Figures 12A and 12B on page 83, line 6 because no Figure 12A or Figure 12B was submitted with the application.

No new matter is introduced by these amendments.

Amendments to the Drawings

In Figure 7A (Formal Drawing 7A-1), the following minor changes have been made: 1) the line demarcating the transmembrane region has been shortened such that it extends only over the L at position 72 and no further; 2) the amino acid number designation "77", at the end of the first line of LT-alpha sequence has been changed to "76"; and 3) the "G" at position 197 of Neutrokine-alpha sequence was changed from being white on black to being black on white. Copies of the original drawing, in both its informal and formal form, are attached with these changes marked in red.

The amendment of the length of the line demarcating the transmembrane region brings the drawing into conformity with the description of the transmembrane region as it is defined in the specification in several locations. See for example page 10, lines 20-23 where the transmembrane region is defined as amino acids 47 to 72 of the Neutrokine-alpha polypeptide. Thus, this amendment introduces no new matter and is fully supported by the specification.

The amendment of the amino acid number designation corrects the numbering of the sequence such that it agrees with the numbering of the sequence of Lymphotoxin-alpha given in Gray, *Nature* 312,721-724 (1984). The Gray *et al.* Nature article is cited on page 412, line 15 of the specification in reference to Figure 7A. GenBank Reports for Accession Numbers CAA25649 and P01374 are submitted in support of this amendment. CAA25649 is the original GenBank submission for the Gray *et al.* article. Because the Gray GenBank report does not identify the lymphotoxin (LT) as LT-alpha, GenBank report P01374, which also cites the Gray *et al.* reference, is also included. Thus, this amendment introduces no new matter and is fully supported by the specification.

The shading of certain amino acid residues in Figure 7 indicates which amino acid residues match the consensus sequence. The amendment of the "G" at position 197 of Neutrokine-alpha sequence corrects the shading because a serine (S), and not a glycine (G) residue is the consensus residue at this position. Support for this amendment is found in Figure 2B (Formal Drawing Figure 2C) where the G at position 197 of the Neutrokine alpha polypeptide is not shaded. Thus, this amendment introduces no new matter and is fully supported by the specification.

CONCLUSION

Applicants respectfully request that the amendments and remarks above be entered and made of record in the file history of the instant application.

Respectfully submitted,

Dated: July 28, 2000

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Attorney for Applicants

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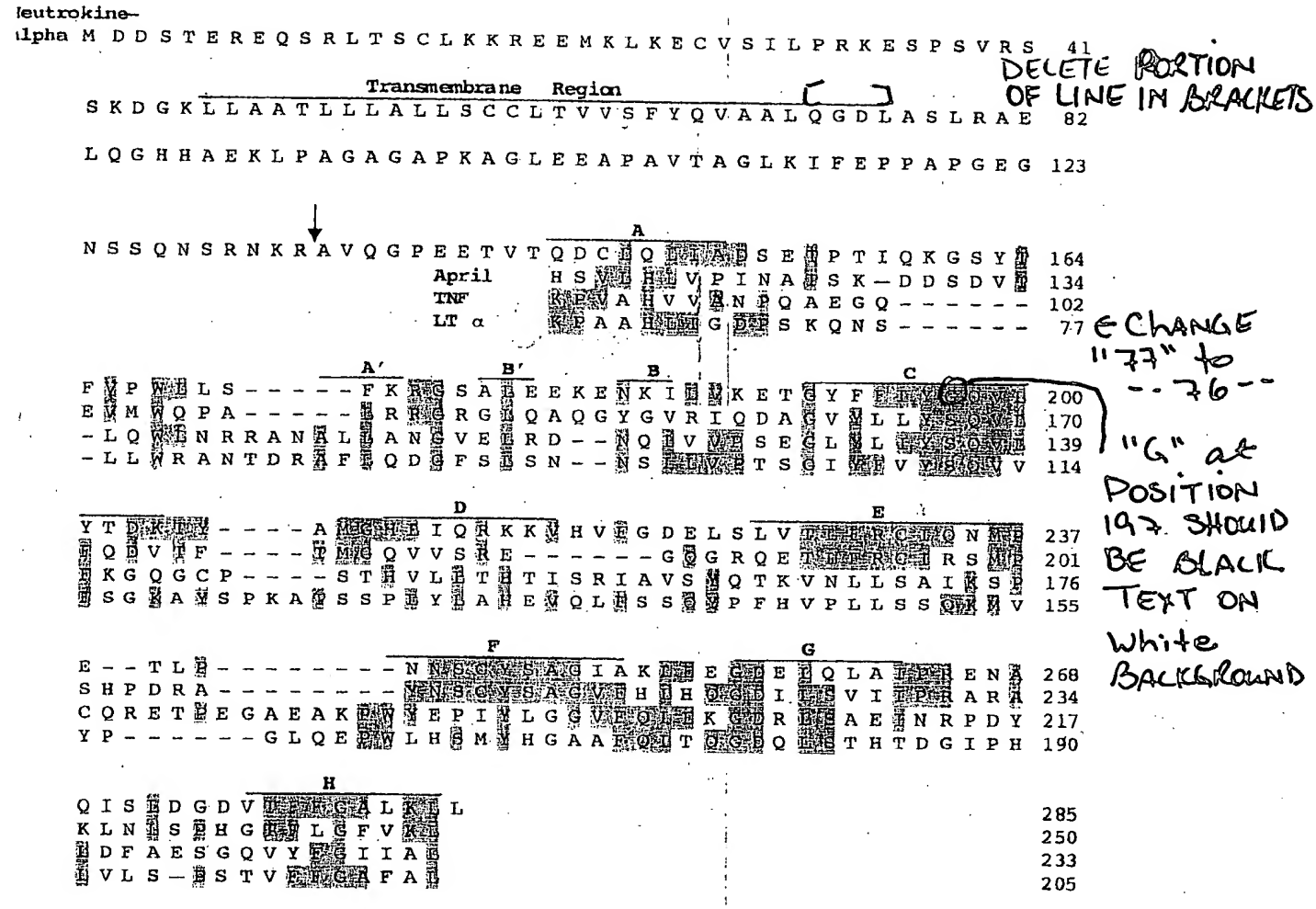
Telephone: (301) 610-5771

Figure 7

a.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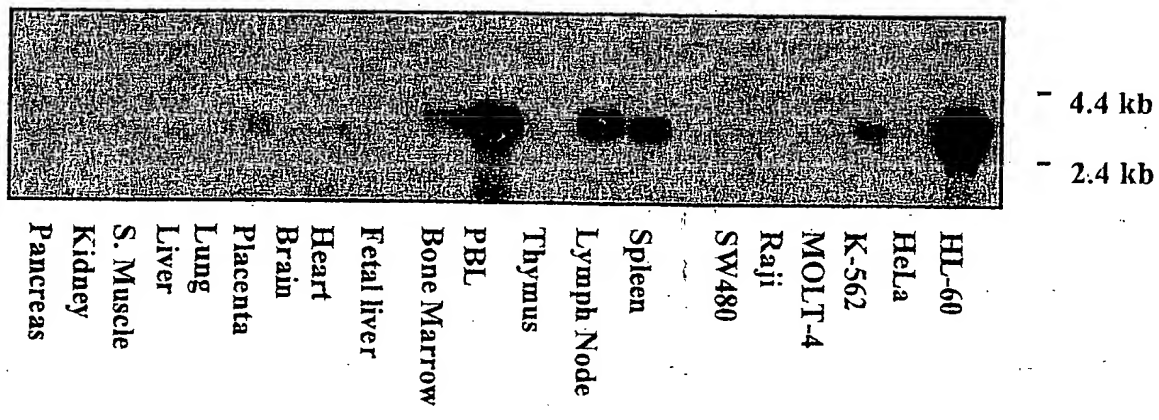
Transmembrane Region
S K D G K L L A A T L L L A L L S C C L T V V S F Y Q V A A L Q G D L A S L R A E 82
L Q G H H A E K L P A G A G A P K A G L E E A P A V T A G L K I F E P P A P G E G 123
N S S Q N S R N K R A V Q G P E E T V T Q D C L Q L I A E S E T P T I Q K G S Y T 164
April H S V T H L V P I N A E S K — D D S D V T 134
TNF K P V A H V V A N P Q A E G Q - - - - - - - 102
LT α K P A A H L T G D P S K Q N S - - - - - - - 77
A
A′
B′
B
C
D
E
F
G
H
DELETE PORTION OF LINE IN BRACKETS
CHANGE "77" to --76--
"G" at POSITION 197 SHOULD BE BLACK TEXT ON White BACKGROUND

b.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Liver
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SW480
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HeLa
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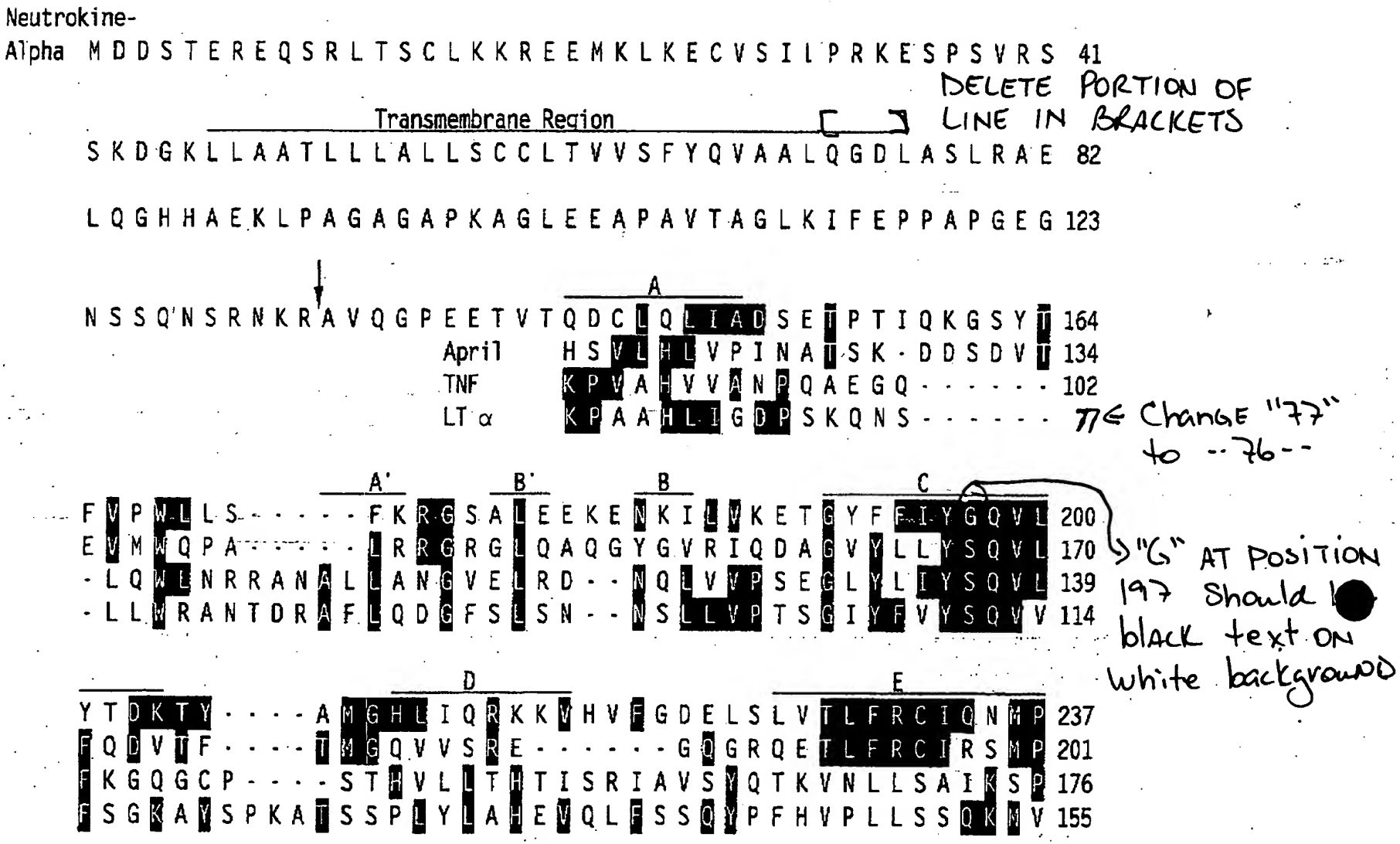
Neutrokine-
Alpha M D D S T E R E Q S R L T S C L K K R E E M K L K E C V S I L P R K E S P S V R S 41
DELETE PORTION OF LINE IN BRACKETS
Transmembrane Region
S K D G K L L A A T L L L A L L S C C L T V V S F Y Q V A A L Q G D L A S L R A E 82
L Q G H H A E K L P A G A G A P K A G L E E A P A V T A G L K I F E P P A P G E G 123
A
N S S Q N S R N K R A V Q G P E E T V T Q D C L Q L I A D S E T P T I Q K G S Y T 164
April H S V L H L V P I N A T S K - D D S D V T 134
TNF K P V A H V V A N P Q A E G Q - - - - - - 102
LT α K P A A H L I G D P S K Q N S - - - - - - 77
Change "77" to --76--
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E V M W Q P A - - - - - L R R G R G L Q A Q G Y G V R I Q D A G V Y L L Y S Q V L 170
- L Q W E N R R A N A L L A N G V E L R D - - N Q L V V P S E G L Y L I Y S Q V L 139
- L L W R A N T D R A F L Q D G F S L S N - - N S L L V P T S G I Y F V Y S Q V V 114
"G" AT POSITION 197 Should be black text ON white background
D E
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F Q D V T F - - - - T M G Q V V S R E - - - - - - G Q G R Q E T L F R C I R S M P 201
F K G Q G C P - - - - S T H V L L T H T I S R I A V S Y Q T K V N L L S A I K S P 176
F S G K A Y S P K A T S S P L Y L A H E V Q L F S S Q Y P F H V P L L S S Q K M V 155

FIG.7A-1

NCBI Entrez Protein

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PID         g34445
VERSION     CAA25649.1  GI:34445
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SOURCE      human.
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            Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 205)
  AUTHORS   Gray,P.W., Aggarwal,B.B., Benton,C.V., Bringman,T.S., Henzel,W.J.,
            Jarrett,J.A., Leung,D.W., Moffat,B., Ng,P., Svedersky,L.P.,
            Palladino,M.A. and Nedwin,G.E.
  TITLE     Cloning and expression of cDNA for human lymphotoxin, a lymphokine
            with tumour necrosis activity
  JOURNAL   Nature 312 (5996), 721-724 (1984)
  MEDLINE   85086243
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VERSION     P01374  GI:135940
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            sequence updated: Mar 1, 1989.
            annotation updated: Nov 1, 1997.
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KEYWORDS    Cytokine; Glycoprotein; Cytotoxin; Signal; Polymorphism.
SOURCE      human.
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            Eutheria; Primates; Catarrhini; Hominidae; Homo.
REFERENCE   1  (residues 1 to 205)
  AUTHORS   NEDOSPASOV,S.A., SHAKHOV,A.N., TURETSKAYA,R.L., METT,V.A.,
            AZIZOV,M.M., GEORGIEV,G.P., KOROBKO,V.G., DOBRYNIN,V.N.,
            FILIPPOV,S.A., BYSTROV,N.S., BOLDYREVA,E.F., CHUVPILO,S.A.,
            CHUMAKOV,A.M., SHINGAROVA,L.N. and OVCHINNIKOV,Y.A.
  TITLE     Tandem arrangement of genes coding for tumor necrosis factor
            (TNF-alpha) and lymphotoxin (TNF-beta) in the human genome
  JOURNAL   Cold Spring Harb. Symp. Quant. Biol. 51 Pt 1, 611-624 (1986)
  MEDLINE   87217060
  REMARK    SEQUENCE FROM N.A.
REFERENCE   2  (residues 1 to 205)
  AUTHORS   Nedwin,G.E., Jarrett-Nedwin,J., Smith,D.H., Naylor,S.L.,
            Sakaguchi,A.Y., Goeddel,D.V. and Gray,P.W.
  TITLE     Structure and chromosomal localization of the human lymphotoxin
            gene
  JOURNAL   J. Cell. Biochem. 29 (3), 171-181 (1985)
  MEDLINE   86086150
  REMARK    SEQUENCE FROM N.A.
REFERENCE   3  (residues 1 to 205)
  AUTHORS   Kobayashi,Y., Miyamoto,D., Asada,M., Obinata,M. and Osawa,T.
  TITLE     Cloning and expression of human lymphotoxin mRNA derived from a
            human T cell hybridoma
  JOURNAL   J. Biochem. 100 (3), 727-733 (1986)
  MEDLINE   87057135
  REMARK    SEQUENCE FROM N.A.
REFERENCE   4  (residues 1 to 205)
  AUTHORS   GRAY,P.W., AGGARWAL,B.B., BENTON,C.V., BRINGMAN,T.S., HENZEL,W.J.,
            JARRETT,J.A., LEUNG,D.W., MOFFAT,B., NG,P., SVEDERSKY,L.P.,
            PALLADINO,M.A. and NEDWIN,G.E.
  TITLE     Cloning and expression of cDNA for human lymphotoxin, a lymphokine
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  JOURNAL   Nature 312 (5996), 721-724 (1984)
  MEDLINE   85086243
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  AUTHORS   Matsuyama,N., Okawa,N., Tsukii,Y., Endo,T. and Kaji,A.
  TITLE     Nucleotide sequence of a cDNA encoding human tumor necrosis factor
            beta from B lymphoblastoid cell RPMI 1788
  JOURNAL   FEBS Lett. 302 (2), 141-144 (1992)
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            PERROT,V., JURKA,J., RODRIGUEZ-TOME,P., CLAVERIE,J.-M., DAUSSET,J.
            and COHEN,D.
  TITLE     Dense Alu clustering and a potential new member of the NF kappa B
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  JOURNAL   Nat. Genet. 3 (2), 137-145 (1993)
  MEDLINE   93272029
  REMARK    SEQUENCE FROM N.A.
REFERENCE   7  (residues 1 to 205)
  AUTHORS   Voigt,C.G., Maurer-Fogy,I. and Adolf,G.R.
  TITLE     Natural human tumor necrosis factor beta (lymphotoxin). Variable
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  JOURNAL   FEBS Lett. 314 (1), 85-88 (1992)
  MEDLINE   93083656
  REMARK    PARTIAL SEQUENCE, CARBOHYDRATE-BINDING SITES, AND VARIANT.
REFERENCE   8  (residues 1 to 205)
  AUTHORS   Eck,M.J., Ultsch,M., Rinderknecht,E., de Vos,A.M. and Sprang,S.R.
  TITLE     The structure of human lymphotoxin (tumor necrosis factor-beta) at
            1.9-A resolution
  JOURNAL   J. Biol. Chem. 267 (4), 2119-2122 (1992)
  MEDLINE   92129275
  REMARK    X-RAY CRYSTALLOGRAPHY (1.9 ANGSTROMS).
REFERENCE   9  (residues 1 to 205)
  AUTHORS   Abraham,L.J., Du,D.C., Zahedi,K., Dawkins,R.L. and Whitehead,A.S.
  TITLE     Haplotypic polymorphisms of the TNFB gene
  JOURNAL   Immunogenetics 33 (1), 50-53 (1991)
  MEDLINE   91139175
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            The original entry is available from http://www.expasy.ch/sprot
            and http://www.ebi.ac.uk/sprot
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            [SUBUNIT] HETEROTRIMER OF EITHER TWO BETA AND ONE ALPHA SUBUNITS OR
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